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14. ABSTRACT

Background: Currently, no established method exists for screening young, pre-menopausal women for breast cancer. Electrical Impedance Scanning (EIS), an innovative breast screening technology, appears to identify women at increased risk for breast cancer.

Aim: A multi-center trial in the North Atlantic Region has been initiated in an effort to extend the potential benefit of this new technology to active-duty service members and young female healthcare beneficiaries with the aim of acquiring the data necessary to determine the feasibility of the EIS system, T-Scan™ 2000ED as a breast cancer risk identifying/screening tool in young women.

Methods: Women age 30 to 45 underwent EIS with routine clinical breast examination. EIS+ women were referred for further diagnostic breast imaging and breast biopsy, if indicated.

Results: 1,385 women were studied. Three women had a high risk or cancerous tumour of the breast; one was T-Scan positive. Of the 1,382 with benign findings, 1,285 were T-Scan negative. Thus, our interim results are consistent with an earlier validation trial showing that a T-Scan positive woman is six times more likely to have a high-risk lesions or cancer (~1 in 100) than a T-Scan negative women (~1 in 600).

Conclusion: Continuation of the present multi-center trial is warranted to confirm that EIS can identify young women at increased risk for breast cancer, those most likely to benefit from more diligent surveillance, early breast imaging, and risk reduction intervention.

15. SUBJECT TERMS
Breast cancer; screening; risk identification; electrical impedance scanning

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Annual Report for Electrical Impedance Scanning (EIS)
For the Early Detection of Breast Cancer
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Introduction

PROBLEM:
Cancer accounts for one third of all illness-related mortality in the United States Army. Breast cancer, specifically, is the most common cancer in women and a leading cause of cancer death among those under the age of 40. Mammography, the gold standard for breast cancer screening in women over 40, is of limited use in younger women who typically have dense breast tissue, which is difficult to visualize with standard mammography. Widespread mammographic screening of younger women is further restricted because of concerns regarding the cumulative dose of radiation to which patients would be exposed on an annual basis.

Due to the limitations of mammography in younger patients, women under age 40 are generally not referred for breast imaging unless they are at elevated risk for breast cancer based upon a known familial risk factor. Unfortunately, 90-95% of breast cancers occur in "average-risk" women without known risk factors such as family history and gene mutations. Thus, a technology like Electrical Impedance Imaging (EIS), which is designed to more consistently and reliably identify "at risk" women by specifically analyzing individual tissue characteristics, would present the clinical community with an opportunity to offer additional surveillance to those 95% of women who are undetected by the current standard of care. The EIS system would thus be used to refer this at-risk subset of women for early breast imaging such as MRI (considered highly accurate in detecting early-stage breast cancer in high-risk young women), further follow-up, and risk-reduction measures (such as taking Tamoxifen).

This technology is of specific interest to us because over 92% of active duty women in the United States Army are under 40 years of age and over 50% are either African American or Hispanic. Race and ethnicity are considered important factors in breast cancer detection because death rates from breast cancer in the Army and in the community at large are higher for African American and Hispanic women than for Caucasian women.

The only standard breast cancer-screening tool for young women is clinical breast exam (CBE); however, CBE suffers from low true-positive and high false-positive rates and is not effective in detecting breast cancer at an early stage. In general, cancers discovered by clinical breast exam tend to be more advanced, and require a treatment regimen that is more aggressive, expensive, demanding and often less successful.

The impact of missed breast cancer in young women is considerable. In fact, women under age 50 account for more than 40% of all life years lost to breast cancer. And, as many studies have shown, the economic, social and emotional costs to families and the community are especially grave when young women die of breast cancer. The impact of this illness is especially significant in a military setting where each patient is also a critical component of our fighting force. Since early detection is critical to improved patient outcomes, the development of methods to promote early detection of breast cancer in younger women is widely recognized as a pressing clinical need.

TECHNOLOGY:
Routine screening with Electrical Impedance Scanning (EIS), a new technology that measures electrical signal flow across breast tissue, is under investigation for the

non-invasive detection of tissue current flow abnormalities associated with an increased risk for the development of breast cancer.

The goal of evaluating young women with EIS is risk identification that leads to additional imaging and early detection of breast cancer before it can be found by the current, decidedly inadequate screening method – clinical breast examination. The T-Scan™ 2000ED is a painless, radiation-free, rapid, no-risk breast-scanning device that is easy to use and doesn't require specialized training to interpret. The device consists of a portable flat screen monitor and a computer. A metal cylinder held in the woman's hand opposite the breast being examined is connected to the computer. A low-level, electrical signal is transmitted from the cylinder up the musculature of the arm, across the pectorals, and through each breast. The electrical current is measured on the breast with a non-invasive surface probe. The final EIS result is binary [suspicious (high-risk) –or– not suspicious (low-risk)], is entirely calculated by the computer software, and is immediately available to the examiner.

Initial results of a study of 2,035 young women undergoing T-Scan™ 2000ED EIS exam along with clinical breast exam indicate that an EIS positive woman is more than six times as likely as the average woman to have breast cancer. Further large-scale studies are needed to confirm that EIS can identify young women at increased risk for breast cancer, those most likely to benefit from more diligent surveillance, early breast imaging, and risk-reduction intervention.

Body

PROPOSED FIELD TESTING:
Breast tissue evaluation with EIS, as incorporated into the T-Scan™ 2000ED system, has enormous potential for our young female healthcare beneficiaries in terms of early detection, survival, active-duty force health promotion and disease prevention. Further testing of this technology is warranted and feasible within the Army based on the unique demographics of the active-duty population and the inherent deficiencies of using clinical breast examination alone to screen young women under the age of 40. This need is especially evident in the African-American and Hispanic patient population, which makes up nearly half of our fighting force.

A five-center, 5-year trial in the North Atlantic Region has been initiated in an effort to assess the potential benefit of this new technology to active-duty service members and young female healthcare beneficiaries with the aim of acquiring the data necessary to determine the feasibility of T-Scan™ 2000ED as a screening tool in young women

STUDY AIMS:
The present IRB-approved clinical trial uses electrical impedance scanning technology (T-Scan™ 2000ED) in order to address a unique research question, *Can tissue-based bioelectrical changes be utilized to reliably identify young women at increased risk of breast cancer?*

STUDY METHODOLOGY:
We have initiated a multi-center prospective clinical study of young women age 30 to 45 years who undergo annual physical cancer screening examinations. Study participants who

have completed informed consent undergo clinical breast exam (CBE), followed by EIS with the latest version of T-Scan™ 2000ED. Women who are positive on T-Scan are referred for further breast imaging, and if indicated as a result of the follow-up procedure, they undergo breast biopsy.

Summary of Results

Five centers (Walter Reed Army Medical Center; DeWitt Army Community Hospital, Ft Belvoir; Kimbrough Ambulatory Care Clinic, Ft Meade; Keller Army Hospital, West Point; Malcolm Grow Air Force Medical Center, Andrews AFB) are participating in this prospective multi-center clinical trial evaluating electrical impedance scanning (EIS) for breast cancer risk identification in young women.

As of December 31, 2005, there were **1,393 women** enrolled in the study. Table 1 demonstrates the ethnic diversity of the study population.

Table 1: Ethnic Origin of Study Participants

American Indian/ Alaskan Native	Asian	Native Hawaiian or Other Pacific Islander	Hispanic	Black	White	Multiracial	Other	Total
8	53	10	76	337	897	11	1	1,393

Adverse Events:

There were no reported cardiac, neurological, dermal, thermal or allergic reactions or adverse events, nor any reports of patient discomfort. This outcome echoed similar findings in the previous pilot (n=1,103) and validation (n=2,035) studies and in more than 10,000 prior examinations with the predecessor T-Scan 2000 device as reported in the previously approved PMA (FDA) application.

Study participant age and follow-up after EIS Screening Exam:

Distribution of study subjects according to age, EIS, radiological referrals (and suspicious findings), and biopsy referrals (and high-risk or cancerous diagnoses) are shown in Table 2.

Table 2: Follow-Up by EIS Outcome and Age

Scan	Age	Total	US	(Susp.)	MX	(Susp.)	MRI	(Susp.)	BX	(High-risk, Cancer)
EIS+	<40	49	8	0	37	0	32	0	0	0
	40+	49	4	0	46	0	37	2	3	1
EIS-	<40	747	47	4	82	4	17	0	5	0
	40+	540	62	6	378	7	21	2	13	2

US – ultrasound; MX – Mammogram; MRI – Magnetic Resonance Imaging; Susp. (Suspicious); BX – breast biopsy

Pivotal findings:

The T-Scan positive rate was 7.1%, with 1,385 women completing the EIS examination. The risk for biopsy-proven cancer or high-risk lesion in T-Scan positive patients is ~1 in 100, six times greater than the ~1 in 600 risk for T-Scan negative patients. Table 3 summarizes the EIS outcomes.

Table 3: EIS Outcomes

EIS result	Cancer or high-risk lesion	No cancer or high-risk lesion	Total
Positive	1	97	98
Negative	2	1,285	1,287
Total	3	1,382	1,385

Interpretation of Results

EIS (T-Scan) Screening Model:

In reviewing the T-Scan breast cancer risk stratification model, a clear and accurate description of the device's clinical utility may be illustrated via a comparative analysis of absolute risk for breast cancer in each of several patient populations. Specifically, absolute risk in the target or intended use population of young women can be compared with the absolute risk in other populations that are typically offered mammography.

It is presumed that if the T-Scan exam can identify women who are at an absolute risk for breast cancer that is equal to or greater than that of older women who are routinely offered mammography, the clinical benefit of this EIS screening approach should be evident.

The Routinely Screened Population, Women over 40:

Breast cancer screening guidelines endorsed by The National Cancer Institute, the American Cancer Society, the American College of Radiology and the U.S. Preventive Services Task Force all recommend annual mammograms for women over 40. The yield of mammographic screening is generally measured as the number of mammograms performed per cancer detected. Measured across the decade between age 40 and 49, approximately 300 to 400 mammograms are performed per detected breast cancer. The absolute risk in this age group is thus ~1 in 350 or approximately 0.0028. This level of absolute risk is therefore considered the "minimal screening threshold".

The Unscreened Population, Women under 40:

The American population of women under 40 accounts for nearly 11,000 breast cancers each year – equal to the total number of all cervical cancers in all ages annually diagnosed in the United States. Nonetheless, the low overall prevalence precludes mammographic screening of average risk women on a routine basis. Specifically, about 1.5 cancers are detected per 1,000 women between age 30-39 yielding an absolute risk of approximately 0.0015,

considerably less than the accepted risk minimal screening threshold for annual mammography screening in women 40+ years of age. Thus women under 40 continue to rely upon clinical breast exam alone for breast cancer screening.

The T-Scan Population, Categorizing Young Women as "Low risk" or "At risk":

By pre-screening average risk women in the target population as part of an annual well woman screening exam, the EIS screening intends to sub-classify (segment) the pool of young women into a "low risk" pool and an "at risk" pool. Importantly, the "at risk" sub-population should be at an absolute risk that is equal to or greater than the risk at which women are routinely screened with mammography, the minimal screening threshold.

Given a sensitivity of 33% and a specificity of 93% for the identification of high-risk lesions or breast cancer as evidenced in the on-going clinical trial and assuming a patient pool of 10,000 patients and 15 cancers (consistent with published prevalence data), T-scan risk stratification would proceed in the following manner:

T-Scan Negative patients, "low risk":

The pool of 10,000 patients yields 9,300 T-Scan Negative patients (93% of 10,000) and includes 10 "missed" cancers (67% of 15). Thus the absolute risk in the low-risk group is 1 cancer per 930 patients or 0.0011. This level of risk is significantly below the average risk in the target population and only a third of the minimal screening threshold.

T-Scan Positive patients, "at risk":

The pool of 10,000 patients yields 700 T-Scan Positive patients (7 % of 10,000) and includes 5 "detected" high-risk lesions or cancers (33% of 15). Thus the absolute risk in the "at risk" group is 1 cancer per 140 patients or 0.0071. This level of risk is significantly above the average risk in the target population and over three times greater than the absolute risk at which we commonly screen women over age 40.

Key Research Accomplishments

INTERIM ANALYSIS:
During the first six months of the five-year trial launched in the summer of 2005 we tested 1,385 young women. Three had a high-risk or malignant tumor of the breast; one was T-Scan positive. Of the 1,382 with benign findings, 1,285 were T-Scan negative. Thus, our interim results are consistent with an earlier validation study of 2,035 young women undergoing T-Scan™ 2000ED EIS exam along with clinical breast exam showing that an EIS positive woman is more than six times as likely as the average woman to have breast cancer.

The interim results of the current study indicate that a T-Scan positive woman is six times more likely to have a high-risk lesion or cancer (~1 in 100) than a T-Scan negative women (~1 in 600).

Reportable Outcomes

FUNDING APPLIED FOR:
Defense Acquisition Challenge Program (DACP) – A proposal to DACP has been submitted in order to allow the continuation and completion of this study.

Conclusions

The findings of the present prospective multi-center NARMC regional breast cancer screening trial are consistent with those of a prior EIS validation study indicating that women undergoing breast cancer screening with positive T-Scan are at increased risk of having breast cancer.

The interim results of the current study indicate that a T-Scan positive woman is significantly more likely to have a high-risk lesions or cancer than a T-Scan negative woman. This level of absolute risk compares favourably to the minimal screening threshold for mammography screening and may justify early breast imaging in women under age 40.

Implications

This study represents an important step involving adaptation of existing EIS technology for use under novel investigational clinical application: T-Scan for the identification of young women at high-risk for breast cancer.

We are exploring the efficacy of using EIS as an integral part of the screening process, a screening process that is widely recognized as deficient currently when examining young women with clinical breast exam alone during periodic office visits to the gynecologist or the primary care physician.

T-Scan is very safe, as there were no reported cardiac, neurological, dermal, thermal or allergic reactions or adverse events, or any reports of discomfort among over 4,000 women studied thus far with this device.

Our healthcare beneficiaries regard screening young women for breast cancer as extremely important, and they are very satisfied with the comfort, safety, and rapidity of T-Scan. The success of this proposed novel-screening paradigm (Breast T-Scan + Clinical Breast Exam, if proven efficacious) will likely increase awareness and compliance of required annual mammographic screening when a women reaches age 40.

More importantly, early detection of breast cancer through EIS-directed risk assessment and early breast imaging would translate into less aggressive treatment, more rapid return to duty, improved quality of life and survival in our young female healthcare beneficiaries.

Recommendations

Continuation of the present multi-center trial is essential to confirm that EIS can indeed consistently identify young women at increased risk for breast cancer – those that are most likely to benefit from more diligent surveillance, early breast imaging, and risk reduction intervention.

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